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Discussion by H. Z. Lund, Western Reserve University, Cleveland, O.

The contrast of appearance of a pigmented nevus of a child and that of an adult is generally known. We have recently made a systematic study of the appearance of benign pigmented nevi at all ages and find that there are, in most instances, progressive changes which roughly correlate with the age of the patient. The most important variables are junctional proliferation which is present to a moderate to marked degree in about 90 per cent. of children under 10 years of age. The subsequent decades show a marked diminution in this percentage but there is no age at which it abruptly ceases. Slight degrees can be found in many nevi in adult life. Mitotic figures are found rarely but likewise show a higher incidence in the first decade and then a steady drop. Mitotic figures are uncommon in adult life. In later life the nevus cells are more fusiform and associated with fibrils. Fibrils progressively increase with age, as do the structures resembling tactile corpuscles. Thus the nevus cells which early in life resemble epithelium gradually differentiate to tissue resembling neuroid structures. There are exceptions to the above trend which cannot be discussed here.

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## Discussion by EUGENE F. TRAUB, New York Medical College.

I am in accord with Dr. Becker that an accurate diagnosis of pigmented nevi is possible only after microscopic examination. Not only are a number of other lesions frequently mistaken for pigmented nevi but the differentiation of one pigmented nevus from the other is often impossible without microscopic examination. Dr. Becker has used a classification for the study of nevi based upon that of Miescher and von Albertini. It is not entirely clear to me just exactly what all may be included in each of his three types. Furthermore, to remember them as types "A," "B" and "C," is rather meaningless unless fully explained by the accompanying text or a specially appended name. But it would seem that each of his types may be a hodge-podge of several varieties of nevi, which is never good. For example, type "A' is exemplified by lesions of an intra-epithelial growth while type "B" includes the "common mole" or intra-dermal nevus of my classification as well as the blue nevus and one would have to specify which of these, or any mixed types, was meant. Dr. Becker admits that depending on where and how the

sections are cut, one might find the lesion fitting into type "A," "B" or even "C." This would not occur in a classification like mine, except in the case of a mixed nevus as, in most instances, there would be no difficulty in recognizing at once if its exact type is intra-epidermal, intra-dermal, junction or blue nevus.

I do not agree with some of the methods of the treatment suggested by Dr. Becker. He suggests that large macular pigmented nevi could be destroyed with solid carbon dioxide, electrocoagulation or by fulguration. I believe some of these procedures are satisfactory for some of the rather small lesions but where larger pigmented nevi are involved, I believe the hair line scar of a surgical excision gives a better cosmetic result than can be accomplished by making a scar of the entire area. This is particularly true with those nevi complicated with hair that requires extensive electrolysis after the pigment is first destroyed with either solid carbon dioxide, electrocoagulation or fulguration. In these cases, it is much simpler to excise the lesion at one sitting, unless it is so large that closure is utterly impossible and even then sometimes skin grafting is preferable to many repeated treatements by electrocoagulation, electrolysis, etc. Furthermore, as Dr. Becker pointed out, diagnostic errors can only be prevented or corrected on study of the tissues and this can best be done only by excising and examining the entire lesion.

## The Problem of Acanthosis Nigricans.

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Acanthosis nigricans is a benign dermatosis showing hyperpigmentation, mostly in the basal cell layer, as well as other characteristic epidermal changes. Warts and pigmented spots or moles may accompany these lesions. About 450 cases of the disease have been reported. The dermatosis is regionally and symmetrically distributed, the axillas being the most commonly involved area. Melanomas do not develop from the lesions. Acanthosis nigricans occurs in man and dog and is found in both sexes. Its significance lies in its association with internal cancer. This combination is seen in 50% of cases of acanthosis nigricans. The type of acanthosis nigricans associated with internal

cancer is falsely called malignant. The type of the disease not so associated is called benign. The two types look alike but can, I believe, be differentiated by careful anal-

ysis.

The cancers associated with acanthosis nigricans are highly malignant, non-pigmented adenocarcinomas originating in the stomach or other abdominal organs in 92%, and in the breast, lung, etc., in 8%. Not a single patient has been cured by treatment of the cancer. The cancers occur mostly in the middle-aged but also in the very young and very old. Acanthosis nigricans may precede the cancer by many years, may start simultaneously with, or it may follow cancer. It appears, therefore, that neither acanthosis nigricans nor cancer causes the other. An activating influence of cancer on acanthosis nigricans, however, cannot be denied.

Acanthosis nigricans not associated with cancer may assume the form of a unilateral pigmented verrucous nevus. It starts at birth, in childhood or at puberty. Sex hormones seem to have a stimulating influence on this benign type of the disease. As in the case of melanoma or certain physiological pigmentations, these patients are subjected at puberty to a physiologic barrage of sex hormones which result in hyperpigmentation and other epithelial changes. Studies of the 17 keto-steroids in young and middle-aged men and women suffering from acanthosis nigricans gave normal values. The parallel action of the cancer agent and the sex hormones on the two types of the dermatosis seems noteworthy.

If an individual develops acanthosis nigricans after puberty he will sooner or later show an internal cancer and the cutaneous disease will become more intense with the manifestation of cancer. Young people, however, may have "malignant" acanthosis nigricans before puberty.

Treatment of the malignant type consists in early recognition and removal of the tumor. In the benign type the lesions sometimes regress spontaneously after puberty.

When it was found that there were no recorded familial cases of the malignant type of acanthosis nigricans, such as had been found in the benign type, an investiga-tion of the genetics of the disease under the auspices of the American Cancer Society was undertaken. Furthermore, in this study an effort is being made to determine whether adenocarcinoma occurs in a higher percentage in the families of patients with acanthosis nigricans than in the ordinary population. Particular difficulties were encountered. In addition to all the known handicaps of genetic studies of cancer in man, one cannot be certain whether cancer victims in the older generations had also shown the cutaneous changes, possibly to a mild degree. If the individual has not yet reached puberty or cancer age, acanthosis nigricans is not likely to be noted. Are genetic carriers of

the dermatosis those with a great number of pigmented moles, and what is the "normal" amount of moles? Genetic carriers of cancer may not have been recognized because family members were not examined for any special metabolic feature on which cancer associated with acanthosis nigricans might be based. Those who transmit the disease might have exhibited such a disturbance to a lesser degree than patients with overt manifestations.

If we should succeed in establishing malignant acanthosis nigricans as a separate disease, a dermatosis might emerge which would, not in 50% but in 100% of cases, be an indicator of internal cancer and might point the way to the biology of certain malig-

nant tumors.

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The Junction Nevus, Forerunner of the Malignant Melanoma and Its Differential Diagnosis from the Standpoint of the Dermatologist.

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The pigmented hairy and warty nevi have always been difficult to classify and no logical clinical classification has ever appeared feasible. Therefore, a simple anatomic basis on which to classify them has given us the best chance to simply describe these lesions and to gain definite knowledge as to which of them are potentially dangerous and which generally remain benign throughout their